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10/581,827	05/23/2007	Quinton Van Rooyen	44.P001	7183

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EXAMINER	
KENNEDY, NICOLETTA	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
03/16/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/581,827	ROOYEN ET AL.	
	Examiner	Art Unit	
	NICOLETTA KENNEDY	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-13* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-11* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1 and 4-13 are currently pending.

Priority

This application, filed June 2, 2006, is a national state entry of PCT/IB04/52616, filed December 1, 2004, and claims foreign priority to South African application 2003/9481, filed on December 5, 2003. Applicants have provided a certified copy of the South African application. The instant claims are supported by the South African application.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 22, 2010 has been entered.

Election/Restrictions

2. Newly submitted claims 12-13 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims are directed to a method for administering a drug transdermally but the claims do not require the patch of claim 1 or the drug of claim 1.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 12-13 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1 and 4-11 are under examination.

Claim Objections

3. Claim 1 is objected to because the lines are crowded too closely together, making reading difficult. Substitute claims with lines one and one-half or double spaced on good quality paper are required. See 37 CFR 1.52(b).

4. Claim 1 is objected to because of the following informalities: there are grammatical errors in claim 1. It is also suggested that the claim be double spaced and then each claim limitation separated by a new line and a semi-colon.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. **Claims 1, 5, 8 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebert et al. (WO 95/24172) (pub. Sept. 14, 1995) in view of Visser et al. (WO 98/56325) (pub. Dec. 17, 1998).**

Independent claim 1 claims a transdermal patch with several features:

(a) a selected irritating substance;

(b) a layered construct adapted to be adhered to the skin;

(c) a defining depot cavity between a proximal and distal layer wherein the proximal layer is in contact with skin and is partially permeable and the distal layer is the outer layer and is impervious to the skin;

(d) a proximal layer that is less permeable to the substance than the skin and is made of elastomeric silicone; and

(e) a composite distal layer comprised of a first layer which is partially permeable to the irritating substance and is comprised of elastomeric silicone material and a second layer which is impervious to the irritating substance;

wherein the patch reduces irritation to the human or animal skin.

Regarding claims 1 and 6, Ebert et al. teach a transdermal delivery device comprising an impermeable backing material laminated to an adhesive layer (abstract and figure). The device further comprises a gelled drug layer between the distal adhesive layer and the proximal adhesive layer (abstract and figure). The adhesive layers are laminated together (p. 6). The backing material may be a silicone elastomer (p. 15). The distal and proximal adhesive layers may be the same and the distal and proximal layers may each be composite layers (p. 17). The distal and proximal layers may be semi-permeable to the drug and the thickness may be adjusted, for example to have quick release from the proximal layer and sustained release from the proximal layer (p. 17). Suitable adhesives include polysiloxanes (p. 16). However, Ebert et al. do not teach that the active agent to be delivered is dimethylformamide (DMF). Visser et al. cure this deficiency.

Visser et al. teach the transdermal administration of dimethylformamide (DMF), a polar compound, to treat a viral or microbial infection (p. 1).

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to have combined the teachings of Ebert et al. with those of Visser et al. to use the transdermal delivery device of Ebert et al. to deliver DMF. One would have been motivated to do so because Ebert et al. teach that the term “drug” or

"pharmacologically active agent" means any chemical or biological material suitable for transdermal administration, including antiinfectives (p. 8-9) and Visser et al. teach that DMF is a drug that may be transdermally delivered to treat viral or microbial infections.

Regarding the functional language of claim 1, the invention as claimed is not structurally distinguishable from the combination of Ebert et al. and Visser et al. and it is therefore the examiner's position that the ability of the permeability of the DMF is less than the permeability of human skin and that the patch reduces the irritation of the human or animal skin. Alternatively, since the permeability of DMF in the human skin is known (Visser et al., p. 27), it would have been within the purview of the skilled artisan to modify the thickness of the proximal and distal layers to adjust permeability, as is suggested by Ebert et al.

Regarding claim 5, Visser et al. teach that the patch may take the form of a disk and may be self-adhesive (p. 19, line 1 and 11).

Regarding claim 8, Visser et al. teach that colloidal silicone dioxide is impregnated with DMF (p. 26).

Regarding claim 11, Ebert et al. teach a method for making a transdermal drug delivery device comprising a proximal peelable film and an adhesive layer (claim 21).

Response to Arguments

Applicant's arguments filed October 4, 2010 have been fully considered but they are not persuasive. Applicant argues that Ebert and Visser do not teach the functional properties as claimed, namely that the proximal layer has a permeability to the irritating substance that is less than the permeability of human or animal skin to the irritating

substance. Applicant argues that Ebert and Visser teach away from this functional property (remarks, p. 6) but provided no basis for this supposition. As stated above, the required structural components of the patch are present and thus, in the absence of evidence to the contrary, the functional properties are presumed met. It is suggested that the features resulting in these functional properties be claimed with more specificity to distinguish from Ebert and Visser.

9. **Claims 1, 4, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebert et al. (WO 95/24172) (pub. Sept. 14, 1995) in view of Visser et al. (WO 98/56325) (pub. Dec. 17, 1998) as applied to claims 1, 5, 8 and 11 and further in view of Landauer et al. (WO 99/13885) (pub. Mar. 25, 1999).**

The combination of Ebert et al. and Vissar et al. teach each limitation of claims 1, 5 and 8. However, they fail to teach the proximal and distal layers the rate of permeability of DMF through the patch. Landauer et al. cure this deficiency.

Regarding claim 4, Landauer et al. teach that the tempo of drug administration is determined by the skin and thus the desorption of the drug through the membrane should be the same or very close to the absorption tempo of the skin (p. 14). Therefore, if the desorption of the drug through the membrane is the same as the absorption tempo of the skin, excess build-up of DMF on the skin of the patient is avoided, thus resulting in less irritation of the human or animal skin.

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to have combined the teachings of Ebert et al. and Visser et al. with those of Landauer et al. to modify the desorption of the drug through the patch to

be the same as the absorption tempo of the skin. One would have been motivated to do so because Visser et al. teach that DMF is a mild to moderate skin irritant (p. 9).

Regarding claim 7, Visser et al. teach that DMF is absorbed through the skin at 9.4 mg/cm^2/hr (p. 27). Landauer et al. teach that the tempo of drug administration is determined by the skin and thus the desorption of the drug through the membrane should be the same or very close to the absorption tempo of the skin (p. 14). Therefore, Landauer et al. teach that the patch may have a permeability of about 9.4 mg/cm^2/hr. MPEP 2144.05 states that "a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties" (quoting *Titanium Metals Corp. of America v. Banner,* 778 F.2d 775, 227 USPQ 774 (Fed. Cir. 1985)). In the instant case, about 9.4 mg/cm^2/hr is so close to 9 mg/cm^2/hr that the patch is expected to have the same permeability properties and reduction in buildup of DMF on the skin of the patient.

Regarding claim 9, Landauer et al. teach that indirect administration of DMF may be done by introducing a known amount of DMF with a syringe into the silicon dioxide adsorbent after the patch has been applied to the skin (p. 17).

Response to Arguments

Applicant's arguments filed October 4, 2010 have been fully considered but they are not persuasive. Please see the above response to arguments. Further, Applicant argues that Landuaer states as a design constraint that the desorption of the drug

through the membrane be the same or very close (remarks, p. 6). However, "very close" allows for less or more than that of skin and less than skin would prevent buildup.

10. **Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ebert et al. (WO 95/24172) (pub. Sept. 14, 1995), Visser et al. (WO 98/56325) (pub. Dec. 17, 1998) and Landauer et al. (WO 99/13885) (pub. Mar. 25, 1999) as applied to claims 1, 4-9 and 11 above, and further in view of Reed (US 5,827,530) (pub. Oct. 27, 1998).**

The combination of Ebert et al., Visser et al. and Landauer et al. teach each aspect of claim 9. While they teach that DMF may be injected into the patch after the patch has been applied to the patient, they fail to teach that there is a self-reclosing nipple or port formation. Reed cures this deficiency.

Regarding claim 12, Reed teaches a fillable transdermal delivery device that utilizes injection ports for post assembly introduction of medicinally active agents (abstract).The fillable reservoir of the transdermal device is filled by means of loading a needle with the active agent and inserting the needle through the septum of the loading port (abstract).

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to have combined the teachings of Ebert et al., Visser et al. and Landauer et al. with those of Reed. to use an injection port for injecting DMF into the patch reservoir. One would have been motivated to do so because this allows the person injecting the DMF to inject the DMF into the reservoir and not into another part of the patch. Further, Reed provide a shield in the interior of the fillable reservoir to protect

the diffusion membrane from damage in the event that the needle is inserted too far (abstract).

Response to Arguments

Applicant's arguments filed October 4, 2010 have been fully considered but they are not persuasive. Applicant argues that claim 10 is distinguished from the prior art because claims 1, 4-9 and 11 are distinguished from the prior art. Because those art rejections are maintained, the rejection of claim 10 is also maintained.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicoletta Kennedy whose telephone number is (571)270-1343. The examiner can normally be reached on Monday through Thursday 8:15 to 6:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Gollamudi Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. K./
Examiner, Art Unit 1611

/Anne R Kubelik/
Primary Examiner, Art Unit 1638